

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listing of claims in the application.

1. (Currently Amended) A modified plasminogen activator inhibitor type-1 (~~“PAI-1”~~) (PAI-1) molecule comprising the amino acid sequence ~~which~~ that is at least 95% identical to SEQ ID NO:2, in which one or more amino acid residues are each substituted by an amino acid residue that contains a sulfhydryl group, such that one or more disulfide bridges are formed at a position selected from the group consisting of ~~between 10-40, 70-120, 150-220, 300-342, 343-350, 351-400~~ 31, 97, 192, 197, 347, and 355, and wherein said modified PAI-1 molecule has ~~an *in vivo*~~ a half-life that is longer than the ~~*in vivo*~~ half-life of a corresponding wild-type PAI-1 molecule, wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator.

2. (Currently Amended) The modified PAI-1 molecule of claim 1 which has an ~~*in vivo*~~ a half-life of ~~over~~ 3 hours, 6 hours, 10 hours, 20 hours, 50 hours, 60 hours, 70 hours, 90 hours, 100 hours, 150 hours, 200 hours, 10 days, 12 days, 16 days, 30 days, or 60 days.

3. (Canceled)

4. (Original) The modified PAI-1 molecule of claim 1 wherein said residue that contains a sulfhydryl group is cysteine.

5. (Currently Amended) A modified plasminogen activator inhibitor type-1 (~~“PAI-1”~~) (PAI-1) molecule comprising the amino acid sequence of SEQ ID NO:2, wherein one or more amino acid residues of SEQ ID NO:2 is substituted by an amino acid residue that contains a sulfhydryl group at positions 31, 97, 192, 197, 347, ~~and~~ or 355, wherein said modified PAI-1 molecule has an *in vivo* a half-life that is longer than the *in vivo* half-life of a corresponding wild-type PAI-1 molecule, and wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator.

6. (Currently Amended) A modified plasminogen activator inhibitor type-1 (~~“PAI-1”~~) (PAI-1) molecule comprising the amino acid sequence of SEQ ID NO:2, wherein one or more amino acid residues is substituted by an amino acid residue that contains a sulfhydryl group at positions (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347, and 355; or (vii) 31, 97, 192, 197, 347, and 355, and wherein said modified PAI-1 molecule has ~~an *in vivo*~~ a half-life that is

longer than the ~~in-vivo~~ half-life of a corresponding wild-type PAI-1 molecule, and wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator.

7. (Canceled)

8. (Canceled).

9. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule inhibits tissue plasminogen activator.

10. (Original) The modified PAI-1 molecule of claim 1 wherein said molecule augments endogenous PAI-1 function.

11. (Currently Amended) A method of producing a modified plasminogen activator inhibitor type-1 molecule said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule ~~comprising a helix D region, an A3 strand, an A4 strand and an A5 strand, said molecule~~ comprising the amino acid sequence ~~which~~ that is at least 95% identical to SEQ ID NO:2, in which one or more amino acid residues are each substituted by an amino acid residue that contains a sulfhydryl group, such that one or more disulfide bridges are formed at a position selected from the group consisting of ~~between 10-40, 70-120, 150-220, 300-342, 343-350, 351-400~~ 31, 97, 192, 197, 347, and 355, ~~and a combination thereof~~, and wherein said modified PAI-1 molecule has ~~an in-vivo~~ a half-life that is longer than the ~~in-vivo~~ half-life of a corresponding wild-type PAI-1 molecule wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

12. (Currently Amended) A method of producing a modified plasminogen activator inhibitor type-1 (~~"PAI-1"~~) (PAI-1) molecule, said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule, said molecule comprising the amino acid sequence of SEQ ID NO:2, wherein one or more amino acid residues of SEQ ID NO:2 are each substituted by an amino acid residue that contains a sulfhydryl group at positions 31, 97, 192, 197, 347, ~~and~~ or 355, wherein said modified PAI-1 molecule has ~~an in-vivo~~ a half life that is longer than the ~~in-vivo~~ half-life of a

corresponding wild-type PAI-1 molecule, wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

13. (Currently Amended) A method of producing a modified plasminogen activator inhibitor type-1 (~~“PAI-1”~~) (PAI-1) molecule, said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding a modified PAI-1 molecule, said molecule comprising the amino acid sequence of SEQ ID NO:2, in which one or more amino acid residues are each substituted by an amino acid residue that contains a sulfhydryl group at positions (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347, and 355; or (vii) 31, 97, 192, 197, 347, and 355, and wherein said modified PAI-1 molecule has ~~an *in-vivo*~~ a half life that is longer than the ~~*in-vivo*~~ half-life of a corresponding wild-type PAI-1 molecule, wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

14. (Currently Amended) A method of treating aberrant angiogenesis in a subject in need thereof, said method comprising administering to a the subject ~~in which such treatment is desired~~ an effective amount of the modified PAI-1 molecule of claim 1.

15. (Rejoinder) A method of treating cancer in a subject suffering therefrom, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

16. (Rejoinder) The method of claim 15 wherein said cancer is selected from the group consisting of breast cancer, colon cancer, ovarian cancer, lung cancer, prostate cancer, melanoma, leukemia, lung cancer, skin cancer, pancreatic cancer, bladder cancer, sarcoma, and uterine cancer.

17. (Canceled).

18. (Canceled).

19. (Canceled)

20. (Canceled).

21. (Withdrawn/Currently Amended) A method of treating ~~uPA-mediated~~ urokinase plasminogen activator-mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

22. (Withdrawn/Currently Amended) A method of treating ~~tPA tissue~~ plasminogen activator mediated fibrinolysis in a subject, said method comprising administering to a subject in which such treatment is desired an effective amount of the modified PAI-1 molecule of claim 1.

23. (Original) A pharmaceutical composition comprising a therapeutically effective amount of the modified PAI-1 molecule of claim 1; and a pharmaceutically acceptable carrier.

24. (Canceled)

25. (Canceled)

26. (Canceled)

27. (Canceled)

28. (Canceled)

29. (Currently Amended) A modified PAI-1 molecule comprising the amino acid sequence of SEQ ID NO:2 wherein amino acid residues at positions: (i) 31 and 97; (ii) 192 and 347; (iii) 197 and 355; (iv) 31, 97, 192, and 347; (v) 31, 97, 197, and 355; (vi) 192, 197, 347 and 355; or (vii) 31, 97, 192, 197, 347, and 355, are substituted with amino acid residues that contain a sulfhydryl group, wherein said modified PAI-1 molecule inhibits urokinase plasminogen activator.

30. (Currently Amended) A method of producing a modified plasminogen activator inhibitor type-1 (~~"PAI-1"~~) (PAI-1) molecule said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding the modified PAI-1 molecule of claim ~~28~~ 1; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

31. (Previously Presented) A method of producing a modified plasminogen activator inhibitor type-1 (~~“PAI-1”~~) (PAI-1) molecule said method comprising:

(a) introducing into a cell a nucleic acid molecule encoding the modified PAI-1 molecule of claim 29; and

(b) culturing the cell under conditions suitable for expression of the modified PAI-1 molecule.

32. (New) The modified PAI-1 molecule of any one of claims 1, 5, and 6, wherein the half-life is an *in vitro* half-life.

33. (New) The modified PAI-1 molecule of any one of claims 1, 5, and 6, wherein the half-life is an *in vivo* half-life.